

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER**      **020895**

**CORRESPONDENCE**



DEPARTMENT OF HEALTH & HUMAN SERVICES

G. Buehler  
Public Health Service

NDA 20-895

Food and Drug Administration  
Rockville MD 20857

Central Research Division  
Pfizer Inc.  
Attention: Sandra J. Croak-Brossman, Ph.D.  
Eastern Point Road  
Groton, CT 06340

OCT 8 1997

Dear Dr. Croak-Brossman:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Viagra (sildenafil citrate) Tablets

Therapeutic Classification: P

Date of Application: September 29, 1997

Date of Receipt: September 29, 1997

Our Reference Number: NDA 20-895

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on November 28, 1997 in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact:

Mr. Gary Buehler  
Regulatory Health Project Manager  
(301) 594-5332

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

Natalia A. Morgenstern  
Chief, Project Management Staff  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Page 2 - NDA 20-895

cc

Orig. NDA

HFD-110

DISTRICT OFFICE

HFD-110/GBuehler;10/1/97

sb/10/1/97;10/7/97

R/D: NMorgenstern/10/1/97

ACKNOWLEDGEMENT - AC



GB  
DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

OCT 31 1997

Pfizer Pharmaceutical Production Corporation  
Attention: Mr. Daniel P. Cronin  
Ringaskiddy  
County Cork  
Ireland

Dear Mr. Cronin:

We acknowledge receipt of your correspondence notifying the Food and Drug Administration of a change of sponsorship of:

Name of Drug: Viagra (sildenafil) Tablets

IND Number: 46,863

Date of Submission: September 18, 1997

Date of Receipt: October 1, 1997

Name of Former Sponsor: Pfizer Central Research

Change in ownership of this IND will require you as the new sponsor to provide:

1. A commitment to amend the IND within 60 days to cover all changes in the IND resulting from new ownership and to provide for subsequent changes by amendments in accord with the IND regulations.
2. A commitment to inform all active investigators of the change and obtain an updated Form FDA 1572 and commitments to you.
3. A list of all active investigators or a statement that they are the same as currently listed in the IND, if this is the case.
4. Any changes in the investigators' curriculum vitae, study protocols or other study parameters.

Page 2 - IND 46,863

All future communications regarding this IND should be forwarded in triplicate, identified with the IND number 46,863 and addressed as follows:

Food and Drug Administration  
Center for Drug Evaluation and Research, HFD-110  
Attention: DOCUMENT CONTROL ROOM  
5600 Fishers Lane  
Rockville, MD 20857

Should you have any questions, please contact:

Mr. Gary Buehler  
Regulatory Health Project Manager  
Telephone: (301) 594-5332

Sincerely yours,

Natalia A. Morgenstern  
Chief, Project Management Staff  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

cc: Pfizer Central Research  
Attention: Sandra Croak-Brossman, Ph.D.  
Eastern Point Road  
Groton, CT 06304-5146

cc:  
Original IND  
HFD-110  
HFD-110/GBuehler;10/23/97  
sb/10/17/97;10/24/97  
R/D: JAdvani/10/23/97  
EBarry/10/23/97  
ADeFelice/10/23/97  
NStockbridge/10/24/97  
NMorgenstern/10/24/97

INFORMATION REQUEST

G. Buehler

JAN 23 1998

NDA 20-895

Pfizer Pharmaceuticals Production Corporation  
c/o Pfizer Central Research Division  
Attention: Sandra J. Croak-Brossman, Ph.D.  
Eastern Point Road  
Groton, CT 06340

Dear Dr. Croak-Brossman:

Please refer to your new drug application (NDA) for Viagra (sildenafil citrate) 25, 50 and 100 mg Tablets.

In reviewing your submission of September 29, 1997, our Medical Officer, Statistician and Biopharmaceuticist raised a number of questions that require your attention. Our comments on your submission are detailed as part of this correspondence (see enclosure).

Sincerely yours,

Natalia A. Morgenstern  
Chief, Project Management Staff  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure

Joint Review - Drs. Stockbridge, Marroum and Mahjoob

cc:

Original NDA

HFD-110

HFD-110/GBuehler/1/23/98

sb/1/23/98

GENERAL CORRESPONDENCE



September 29, 1997

Raymond J. Lipicky, M.D., Director  
Division of Cardio-Renal Drug Products  
Center for Drug Evaluation and  
Research HFD #110  
ATT: DOCUMENT CONTROL ROOM #16B-30  
5600 Fishers Lane  
Rockville, MD 20857

Dear Doctor Lipicky:

**RE: New Drug Application # 20-895 - VIAGRA™ (sildenafil citrate) Tablets**  
**IND - # 46,863 / User Fee ID # 3303**

Pursuant to Paragraph 505(b) of the Federal Food, Drug and Cosmetic Act, and 21 CFR 314.1, we are submitting herewith a New Drug Application (#20-895) for VIAGRA™ (sildenafil citrate) Tablets. Pfizer, Inc. is filing this NDA on behalf of Pfizer Pharmaceuticals Production Corporation, Ringaskiddy, County Cork, Ireland.

The chemistry, preclinical, and clinical data obtained during the investigation of VIAGRA™ under IND- have been organized in this Application in accord with the requirements as currently set forth under 21 CFR 314.50. This Application is also provided in electronic format as discussed and agreed with the Division on May 28, 1997. Text and image information supplied electronically is identical to that provided by paper. Please note, however, that case report forms (CRFs) and case report form tabulations are only being supplied electronically, in accordance with a waiver granted by CDER (reference letter of Dr. Janet Woodcock dated April 24, 1997, attached).

The location of the various sections of this Application, number of volumes being submitted, and other explanatory notes are listed in Attachment 1 of this letter.

The manufacturing site identified in this Application is located in Brooklyn, NY. As such, the Sponsor hereby certifies that a field copy of portions of this Application has been provided to the FDA district office in Brooklyn, NY, and that it is an exact copy of the Chemistry, Manufacturing and Controls section, FDA Form 3439 and the Application Summary contained in the archival and review copies of this NDA.

VIAGRA™ is a selective inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5) and is indicated for the treatment of erectile dysfunction. The physiological mechanism responsible for erection of the penis involves the release of nitric oxide (NO) in the corpus cavernosum in response to sexual stimulation. Nitric oxide activates the enzyme guanylate cyclase, which results in locally increased levels of cGMP, thereby producing smooth muscle relaxation in the corpus cavernosum and allowing inflow of blood. By inhibiting PDE5, VIAGRA™ enhances the normal physiological action of nitric oxide/cGMP, thereby allowing patients with erectile dysfunction to obtain erections adequate for sexual intercourse.

Central Research

Department of Clinical Research

CONFIDENTIAL/TRADE SECRET INFORMATION  
SUBJECT TO 18-USE-1905 AND TO WHICH ALL  
CLAIMS OF PRIVILEGE AND CONFIDENTIALITY  
ARE ASSERTED IN BOTH DISSEMINATION MAY  
ONLY BE MADE WITH THE EXPRESS WRITTEN  
PERMISSION OF PFIZER STATUTORY AND  
COMMON LAW. FURTHER INC.

Dr. Lipicky, M.D., Director  
NDA-20-895

This NDA contains safety data from a total of 4213 subjects enrolled in Phase II/III clinical trials and an additional 576 subjects treated with sildenafil in Phase I clinical trials. Separate safety summaries are provided for 194 subjects participating in studies conducted in Japan and 281 subjects treated in Phase II/III studies with study designs which did not allow them to be incorporated into other groupings. Thus a total of 4526 subjects have received sildenafil and 2091 have received placebo in the clinical development program. The safety data base includes 559 subjects treated for at least one year.

As previously agreed upon with the Agency, the primary endpoints of the pivotal studies are questions # 3 and # 4 of the International Index of Erectile Function (IIEF) questionnaire. Data in this NDA establish the safety and efficacy of VIAGRA™ in the treatment of erectile dysfunction. Four randomized, double-blind, placebo-controlled, multi-centered trials provide substantial evidence of efficacy. In addition, two key supportive studies clearly provide proof of efficacy in patients with diabetes mellitus and patients with spinal cord injury.

Sildenafil, a new chemical entity, is the first oral treatment for erectile dysfunction and thus offers a substantial advantage over the currently available treatments for erectile dysfunction. Accordingly, and as previously discussed and agreed with the Agency, we are requesting a Priority Review for this Application.

Currently, sildenafil is not marketed in any country. Marketing Applications for sildenafil will be filed in Canada, the European Medicinal Evaluation Agency (EMA) utilizing the centralized procedure, and eventually other countries.

In accordance with the requirement of the Generic Drug Enforcement Act of 1992, and in connection with this Application, to the best of its knowledge, Pfizer Inc did not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act.

Please be advised that the applicable user fee for this submission has been remitted in accordance with the Prescription Drug User Fee Act of 1992. We believe NDA-20-895 to be complete for review by the Division and look forward to working closely with the Division.

Should you have any questions regarding the organization or content of this Application, please contact Dr. Sandra J. Croak-Brossman at (860) 441-1903 (phone) or (860) 441-0870 (fax).

Sincerely yours,



Steven W. Ryder, M.D.  
Vice President  
U.S. Clinical Operations



Sandra J. Croak-Brossman, Ph.D.  
Associate Director  
Regulatory Strategy & Registration

enclosures  
Serial No. 000

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